TRANSMITTAL OF APPEAL BRIEF (Large Entity)	Docket No. PA9902

In Re Application Of: **Nicholas Thomas**

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
09/914,603	January 9, 2002	Jeanine Anne Goldberg	22840	1634	7928

Invention: **Analysis of Differential Gene Expression**

COMMISSIONER FOR PATENTS:

Transmitted herewith in triplicate is the Appeal Brief in this application, with respect to the Notice of Appeal filed on **May 6, 2005.**

The fee for filing this Appeal Brief is: **$500.00**

☐ A check in the amount of the fee is enclosed.

☒ The Director has already been authorized to charge fees in this application to a Deposit Account.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. **502-590**

☐ Payment by credit card. Form PTO-2038 is attached.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Signature

Dated: **June 30, 2005**

Yonggang Ji
Amersham Biosciences Corp
Patent Department
800 Centennial Avenue
Piscataway, New Jersey 08855

(732) 980-2875
Reg. No.: 53,073

cc:

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on **June 30, 2005**.
(Date)

Signature of Person Mailing Correspondence

Melissa Leck

Typed or Printed Name of Person Mailing Correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appl. No.	:	09/914,603	Confirmation No.: 7928
Applicant	:	Nicholas Thomas	
Filed	:	January 9, 2002	
TC/A.U.	:	1634	
Examiner	:	Jeanine Anne Goldberg	
Docket No.	:	PA9902	
Customer No.	:	22840	

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

June 30, 2005

APPEAL BRIEF

Sir:

Appellants submit this Appeal Brief in triplicate, appealing from the January 4, 2005, rejection of the Examiner, finally rejecting claims 1-13 and 15-17 in the captioned application. The Notice of Appeal was filed on May 6, 2005, which contained authorization to charge the "Appeal Fee" to Appellants' Deposit Account.

Real Party in Interest

Amersham Pharmacia Biotech, Inc. and Amersham plc, co-owners of the captioned application, are the real parties in interest to this appeal.

Related Appeals and Interferences

There are no other appeals or interferences related to the instant appeal.

Status of Claims

Claims 1–13 and 15-17 are pending in the captioned application and are currently under examination. Claims 1–13 and 15-17 are appealed and are reproduced in Appendix A, attached hereto.

Status of Amendments

Appellants did not request any amendment after Examiner's final rejection of all claims.

Summary of Invention

The instant invention relates to methods for detecting the differential expression or presence of two analytes, and more specifically to procedures which provide for rapid and efficient analysis of gene expression in biological systems. In particular, the invention provides a method of detecting and analyzing differences between nucleic acids from two sources, which method comprises: (1) providing nucleic acids from two sources as labeled probes, wherein the nucleic acids from each source are labeled with a distinct marker; (2) forming a mixture of the labeled probes with pooled reagents wherein each reagent is a population of beads carrying a polynucleotide target, the target of one reagent being different from the target of another reagent, the beads of one reagent being distinguishable from the beads of another reagent; (3) incubating the mixture under

conditions to promote specific hybridization between probes and targets; and, (4) analyzing beads in the mixture by flow cytometry.

Independent claim 1 and claims 2-13 and 15-17 depending thereon, are directed to the bead base nucleic acid analysis methods discussed by Appellants at page 3, line 22, through page 5, line 2, of the specification.

Issues

1. **Whether claims 1-4, 6-13 and 15-17 are properly rejected under 35 U.S.C. § 102(e) as being anticipated by Beattie et al. (US Pat. 6,268,147, July 2001).**
2. **Whether claim 5 is properly rejected under 35 U.S.C. § 103(a) as being unpatentable over Beattie et al. (US 6,268,147, July 2001) in view of Cocuzza et al. (US Pat. 5,484,701, January 1996).**

Grouping of Claims

All of the rejected claims in the rejection appealed hereunder stand or fall together.

Argument

1. **Claims 1-4, 6-13 and 15-17 are not properly rejected under 35 U.S.C. 102(e) § as being anticipated by Beattie et al. (US 6,268,147, July 2001).**

In a final office action dated January 4, 2005, the Examiner has rejected claims 1–4, 6-13 and 15-17 under 35 U.S.C. § 102(e) as being clearly anticipated by Beattie et al.

(US 6,268,147, July 2001). Specifically, the Examiner states, "Beattie et al. (herein referred to as Beattie) teaches a method of nucleic acid analysis using tandem hybridization on color-coded microspheres and flow cytometric detections (Example 18)(limitations of Claim 14). Beattie teaches that the stacking hybridization approach is applicable to "bead technology" where different capture probe sequences are tethered to microspheres which are distinguishable by any measurable (detectable) unique physical or chemical property associated with each bead, such as size, shape, mass, spectral profile, chemical reactivity, electronic properties, etc (col. 38, lines 35-43)(limitations of Claim 8-12,16-17). Beattie teaches that the nucleic acid analyte is annealed with a labeled stacking probe of sequence and length designed to bind to a unique position within the analyte nucleic acid (col. 38, lines 60-64)".

MPEP 2131 provides:

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

"The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Appellants respectfully submit that Examiner is of the opinion that since the claims are drawn to "comprising methods", the claims do not exclude the use of stacking probes. Examiner is of the opinion that therefore the claims are anticipated. Appellants

respectfully disagree. Appellants submit that while Appellants' claims are drawn to "comprising methods" and could encompass additional elements, Beattie does not anticipate Appellants' claims.

Appellants respectfully submit that Beattie clearly does not teach each and every limitation of the claims of the present invention. Furthermore, Beattie fails to disclose, teach or suggest the present invention. Beattie describes a method for nucleic acid analysis using tandem hybridization on color-coded microspheres and flow cytometric detection (Example 18, columns 38–40, Figure 15A and 15B). The method of Beattie requires hybridization of three molecules, (a) a labeled stacking probe, (b) a probe on the bead, and (c) a nucleic acid to be analyzed. The labeled stacking probe hybridizes in tandem with the probe on the bead to the nucleic acid molecules being analyzed. The hybridization product is then analyzed by flow cytometry and detection of label on the stacking probe (Figure 15A and 15B).

Appellants submit that Beattie fails to disclose a method comprising the step of "providing the nucleic acids from two sources as labeled probes" (claim 1 of the instant application). Beattie instead provides a labeled stacking probe, for the detection of the hybridization event. Beattie does not provide nucleic acids from two sources (or target in Beattie) as labeled probes. The current invention is therefore clearly distinct from Beattie. In addition, Appellants direct the Examiner's attention to Figures 2, 3 and 4 of the instant application, as well as to Appellants' description that "mRNAs or cDNAs prepared from control and test cells or tissues are labeled with fluorescent tags to identify their source"

(page 4, lines 20-21). It is clear that Beattie et al. does not teach a method comprising the step of "providing the nucleic acids from two sources as labeled probes" (claim 1 of the instant application). For this reason the rejection is improper.

In view of the foregoing, Appellants respectfully submit that the Examiner's rejection cannot be sustained and should be withdrawn.

2. Claim 5 is not properly rejected under 35 U.S.C. § 103(a) as being as being unpatentable over Beattie et al. (US 6,268,147, July 2001) in view of Cocuzza et al. (US Pat. 5,484,701, January 1996).

The remaining issue is whether Appellants' claim 5 is rendered obvious over Beattie et al. in view of Cocuzza et al. (US 5,484,701), and thus are not patentable under 35 U.S.C. § 103(a).

Appellants believe that the asserted references do not render obvious the Appellants' claim. As stated above, Appellants submit that there is a fundamental difference between the current invention and that of Beattie et al. As such, even if the references are combined, the combination does not render obvious Appellants' claim 5.

In view of the foregoing, Appellants respectfully submit that the Examiner's rejection cannot be sustained and should be withdrawn.

Conclusion

In view of the foregoing, Appellants respectfully assert that the Examiner's rejection cannot be sustained and respectfully requests the reversal of the rejection.

Respectfully submitted,

Yonggang Ji
Registration No.: 53,073
Agent for Appellants

Amersham Biosciences Corp
800 Centennial Avenue
P. O. Box 1327
Piscataway, New Jersey 08855-1327

Tel: (732) 980-2875
Fax: (732) 457-8463

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Appeal Brief – Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on June 30, 2005.

Signature:

Name: Melissa Leck

APPENDIX A

The Rejected Claims

Claim 1 (previously presented): A method of detecting and analyzing differences between nucleic acids from two sources, which method comprises:

a. providing the nucleic acids from two sources as labeled probes wherein the nucleic acids from each source are labeled with a distinct marker;

b. forming a mixture of the labeled probes with pooled reagents of at least two reagents wherein each of the pooled reagents comprises a population of beads carrying a polynucleotide target of known sequence, the polynucleotide target of any one of the pooled reagents being different from the target of any other of the pooled reagents and the beads of any one of the pooled reagents being distinguishable from the beads of any other of the pooled reagents by flow cytometry;

c. incubating the mixture under conditions to promote specific hybridization between probes and targets; and

d. analyzing beads in the mixture by flow cytometry to determine the identity of each bead and to quantify the relative abundance of each target sequence in the two sources.

Claim 2 (original): The method of claim 1 wherein the nucleic acids from two sources are mRNA or cDNA from cells or tissues.

Claim 3 (previously presented): The method of claim 1 wherein the polynucleotide targets are cDNA derived from cellular mRNA.

Claim 4 (previously presented): The method of claim 1 wherein the polynucleotide targets are PCR amplimers.

Claim 5 (previously presented): The method of claim 1 wherein the polynucleotide targets contain terminal biotin groups through which they are attached to streptavidin-coated beads.

Claim 6 (previously presented): The method of claim 1 wherein the polynucleotide targets are single-stranded nucleic acids.

Claim 7 (previously presented): The method of claim 1 wherein the nucleic acids are single-stranded nucleic acids.

Claim 8 (previously presented): The method of claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by size.

Claim 9 (previously presented): The method of claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by the nature of one or more markers attached to the beads.

Claim 10 (previously presented): The method of claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by the concentration of one or more markers attached to the beads.

Claim 11 (previously presented): The method of claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by the size and/or by the nature and the concentration of one or more markers attached to the beads.

Claim 12 (previously presented): The method of claim 9 wherein the markers are fluorescent markers attached to the beads.

Claim 13 (previously presented): The method of claim1 wherein each of the nucleic acids is labelled with a fluorescent tag to indicate its source.

Claim 14 (cancelled)

Claim 15 (previously presented): The method of claim 1 further comprising the step of analysing the data obtained by flow cytometry to yield information about the relative and/or absolute abundances of individual nucleic acid sequences contained within the nucleic acids from two sources.

Claim 16 (previously presented): The method of claim 10 wherein the markers are fluorescent markers attached to the beads.

Claim 17 (previously presented): The method of claim 11 wherein the markers are fluorescent markers attached to the beads.